REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application. Applicants request reconsideration of the subject application based on the following remarks.

Claims 94 and 108-120 are currently pending in the application. Claims 94 and 117-120 have been amended and claims 115-116 have been cancelled without prejudice or disclaimer. Support for the amendments to claim 94 can be found throughout the application as filed. No new matter has been introduced by the instant amendments.

Claim 94 stands rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Sakanaka.

Claims 94, 108-109, and 115-120 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Sakanaka.

Claim 94 stands rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Masahiro.

Claims 94, 108-109, and 115-120 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Masahiro.

As the references are understood, Sakanaka and Masahiro recite that crude saponin fraction(s) of ginseng and ginsenoside Rbl when administered by the dosage and administration routine disclosed therein have the effect of preventing brain ischemia. Thus, the subject matter of Sakanaka and Masahiro is substantially as described in Wen et al., Acta Neuropathol (1996) 91:15-22, which document was filed as part of the IDS submitted on March 25, 2004. Thus, for example, Figure 2 of Wen and Figure 6 of Masahiro recite the same data, e.g., administration of

50 mg and 100 mg of CGS and CGNS. Because Masahiro and Sakanaka provide substantially identical disclosures, the rejection based on each reference will be addressed in combination.

The Wen publication teaches that crude saponin fraction(s) of ginseng are effective for prevention of brain ischemia when administered interperitoneally at a dose of 50mg/kg/day or 100mg/kg/day before the expression of brain ischemia and that ginsenoside Rbl is effective for prevention of brain ischemia when administered interperitoneally at a dose of 10mg/kg/day or 20mg/kg/day.

Thus, Sakanaka and Masahiro teach that elevated doses of crude saponin fraction(s) of ginseng and ginsenoside Rbl recited by Masahiro and Sakanaka may be effective to cerebrovascular disorder or cerebral infarction by the dosages recited *supra*. Moreover, each of Masahiro, Sakanaka and Wen that with regard to the dosage for the preventive effect of crude saponin fraction(s) of ginseng, 100mg/kg/day is superior to 50mg/kg/day, and with regard to ginsenoside Rbl, 20mg/kg/day is superior to 10mg/kg/day.

Further, Wen also teaches that crude saponin fraction(s) of ginseng and ginsenoside Rbl do not show therapeutic effect when administered interperitoneally after the expression of brain ischemia (see Acta Neuropathol, p.19, left column line 3-4).

Thus, for at least the reasons cited above, one skilled in the art would not have been motivated to decrease the dosages below the ranges recited in Sakanaka and Masahiro. The office action cites to MPEP§2144.05 Part II A for the premise that modification of dosage amount is routine experimentation. However, the instant claims provide methods of treatment of or prevention of diseases causing apoptosis or apoptosis-like death of cells by administration of a doses or dosages of ginseng extracts are adjusted to between 145 pg/kg/day and 1450 µg/kg/day, and those of ginseng components are adjusted to between 1.67 pg/kg/day and 1.67 mg/kg/day. The dose or dosage provided by claim 94, as amended, is at least one order of magnitude lower than those recited in Sakanaka or Masahiro. Moreover, Sakanaka and Masahiro teach that higher

dosages provide greater therapeutic effect. Thus, although some modification of dosage may be reasonable, at the time the invention was made, one of ordinary skill in the art would have been directed by the teaching and suggestion of Sakanaka or Masahiro to increase, not decrease, the dosage of red ginseng to a patient susceptible to ischemia.

In contrast, Applicants have surprisingly discovered that mammals suffering from spinal cord injury or cerebral infarction can be treated by administration of crude saponin fraction(s) of ginseng and/or ginsenoside Rbl (which is one of the ginsenoside compositions) at unprecedented low dosage.

Therefore claim 94, as amended, is patentable and non-obvious over Sakanaka, Masahiro, or any combination thereof. Claims 108, 109, and 117-120 depend from claim 94 and are therefore also patentable over Sakanaka, Masahiro, or any combination thereof.

Claim 94 stands rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Zhang.

Claims 94, 108-109, and 115-120 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Zhang.

As the reference is understood, Zhang teaches the amelioration to cerebral infarction by intravenous administration of ginsenoside Rbl at a dose of 10mg/kg/day or 40mg/kg/day. However Zhang recites that ginsenoside Rbl administered at 10mg/kg/day provides only a preventive benefit and that administration at 40 mg/kg/day provides preventive and slight therapeutic benefit. Thus, Zhang teaches that increased dosages of ginsenoside Rbl are preferred for treatment and prevention of cerebral infarction such that one skilled in the art would not have been motivated to increase therapeutic or preventative effect by reducing the administered dosage.

In contrast, Applicants have surprisingly discovered a decent effect on cerebral infarction rat by intravenous administration of an unprecedentedly low dose of 20μ g/kg/day or 200μg/kg/day. Thus, Applicants have discovered that at dosages of 20μ g/kg/day or 200μg/kg/day decrease the lesion size of cerebral infarction by one third to one fourth relative to a control lesion. Furthermore, said therapeutic effect is obviously superior to the effect shown by Zhang et al.

One skilled in the art would not have found motivation from the Zhang disclosure to reduce the dosage of ginsenoside Rb1 to a patient to provide superior therapeutic effect at least because Zhang teaches that higher doses of ginsenoside Rb1 offer superior therapeutic effect against cerebral infarction.

Therefore claim 94, as amended, is patentable and non-obvious over Zhang. Claims 108, 109, and 117-120 depend from claim 94 and are therefore also patentable over Zhang.

Claim 94 stands rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Tamiko.

Claims 94, 108-109, and 115-120 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Tamiko.

Claim 94, as amended, is patentable over Tamiko. Claims 108, 109, and 117-120 depend from claim 94 and are therefore also patentable over Tamiko.

The claims, as amended, provide methods of treating a mammal suffering from or susceptible to diseases causing apoptosis or apoptosis-like death of cells, except for treatment of immune deficiency, which comprises administering to the mammal a composition comprising **ginseng extracts, or ginseng components,** its metabolites; or salts thereof. Thus, the claims, as

amended, do not provide methods of treatment comprising administration of ginseng. Therefore claims 94, 108, 109, 117-120 are patentable over Tamiko.

Reconsideration and allowance of claims 94 and 108-120 is respectfully requested in view of the foregoing discussion. This case is believed to be in condition for immediate allowance. Applicant respectfully requests early consideration and allowance of the subject application.

If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105.**

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned agent would appreciate the opportunity to do so.

Respectfully submitted,

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John B. Alexander (Reg. No.: 48,399)
EDWARDS & ANGELL, LLP
Intellectual Property Group
P.O. Box 55874
Boston, MA 02205
Tel. (617) 439-4444

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